

WHAT IS CLAIMED IS:

1. An isolated nucleic acid molecule comprising a nucleotide sequence that encodes a HKNG1 gene product comprising:
  - (a) the amino acid sequence of SEQ ID NO:2;
  - (b) the amino acid sequence of SEQ ID NO:4;
  - (c) the amino acid sequence of SEQ ID NO:39;
  - (d) the amino acid sequence of SEQ ID NO:41;
  - (e) the amino acid sequence of SEQ ID NO:43;
  - (f) the amino acid sequence of SEQ ID NO:45;
  - (g) the amino acid sequence of SEQ ID NO:49; or
  - (h) the amino acid sequence of SEQ ID NO:66.
2. The isolate nucleic acid molecule of Claim 1, wherein the isolate nucleic acid molecule comprises:
  - (a) the nucleotide sequence of SEQ ID NO:1;
  - (b) the nucleotide sequence of SEQ ID NO:3;
  - (c) the nucleotide sequence of SEQ ID NO:7;
  - (d) the nucleotide sequence of SEQ ID NO:34; or
  - (e) the nucleotide sequence of SEQ ID NO:35.
3. The isolated nucleic acid molecule of Claim 1, wherein the isolated nucleic acid molecule comprises:
  - (a) the nucleotide sequence of SEQ ID NO:38;
  - (b) the nucleotide sequence of SEQ ID NO:40;
  - (c) the nucleotide sequence of SEQ ID NO:42; or
  - (d) the nucleotide sequence of SEQ ID NO:44.
4. The isolated nucleic acid molecule of Claim 1, wherein the isolated nucleic acid molecule comprises:
  - (a) the nucleotide sequence of SEQ ID NO:46;
  - (b) the nucleotide sequence of SEQ ID NO:47; or
  - (c) the nucleotide sequence of SEQ ID NO:48.
5. An isolated nucleic acid molecule consisting of a nucleotide sequence that encodes a mature HKNG1 protein having the amino acid sequence of SEQ ID NO:51.

6. An isolated nucleic acid molecule which hybridizes to the complement of the nucleic acid molecule of any one of claims 1-5 under highly stringent conditions comprising washing in 0.1xSSC/0.1% SDS at 68°C.
7. An isolated nucleic acid molecule which hybridizes to the complement of the nucleic acid molecule of any one of claims 1-5 under stringent conditions comprising washing in 0.2xSSC/0.1% SDS at 50-65°C.
8. The isolated nucleic acid molecule of Claim 6 or 7, wherein said isolated nucleic acid molecule encodes a functionally equivalent HKNG1 gene product.
9. A vector comprising the nucleotide sequence of any one of Claims 1-5.
10. An expression vector comprising the nucleotide sequence of any one of Claims 1-5 operatively associated with a regulatory nucleotide sequence controlling the expression of the nucleotide sequence in a host cell.
11. A host cell genetically engineered to contain the nucleotide sequence of any one of Claims 1-5.
12. A host cell genetically engineered to express the nucleotide sequence of any one of Claims 1-5 operatively associated with a regulatory nucleotide sequence controlling expression of the nucleotide sequence in said host cell.
13. An isolated polypeptide comprising the amino acid sequence of a HKNG1 gene product having:
  - (a) the amino acid sequence of SEQ ID NO:2;
  - (b) the amino acid sequence of SEQ ID NO:4;
  - (c) the amino acid sequence of SEQ ID NO:39;
  - (d) the amino acid sequence of SEQ ID NO:41;
  - (e) the amino acid sequence of SEQ ID NO:43;
  - (f) the amino acid sequence of SEQ ID NO:45; or
  - (g) the amino acid sequence of SEQ ID NO:49;
  - (h) the amino acid sequence of SEQ ID NO:66.
14. An isolated polypeptide consisting of a mature HKNG1 gene product having the amino acid sequence of SEQ ID NO:51.

15. An isolated polypeptide comprising an amino acid sequence encoded by the isolated nucleic acid molecule of Claim 6 or 7.
16. An antibody which selectively binds to the HKNG1 gene product of any one of Claims 13 or 14.
17. A method for treating a HKNG1-mediated disorder in an individual comprising administering to the individual a compound which modulates the expression of an HKNG1 gene in the individual.
18. The method of Claim 17, wherein the compound inhibits or potentiates the expression of an HKNG1 gene in the individual.
19. The method of Claim 17, wherein the compound is a small molecule.
20. The method of Claim 17, wherein the HKNG1-mediated disorder is a neuropsychiatric disorder.
21. The method of Claim 17, wherein the neuropsychiatric disorder is bipolar affective disorder or schizophrenia.
22. The method of Claim 17, wherein the HKNG1 gene encodes a HKNG1 gene product comprising:
  - (a) the amino acid sequence of SEQ ID NO:2;
  - (b) the amino acid sequence of SEQ ID NO:4;
  - (c) the amino acid sequence of SEQ ID NO:39;
  - (d) the amino acid sequence of SEQ ID NO:41;
  - (e) the amino acid sequence of SEQ ID NO:43;
  - (f) the amino acid sequence of SEQ ID NO:45;
  - (g) the amino acid sequence of SEQ ID NO:49;
  - (h) the amino acid sequence of SEQ ID NO:51;
  - (i) the amino acid sequence of SEQ ID NO:64; or
  - (j) the amino acid sequence of SEQ ID NO:66.
23. The method of Claim 17, wherein the individual is a mammal.
24. The method of Claim 23, wherein the mammal is a human.

25. A method for treating a HKNG1-mediated disorder in an individual comprising administering to the individual a compound which modulates the expression or activity of a HKNG1 gene product in the individual.
26. The method of Claim 25, wherein the compound inhibits or potentiates the expression or activity of a HKNG1 gene product in the individual.
27. The method of Claim 25, wherein the compound is a small molecule.
28. The method of Claim 25, wherein the HKNG1-mediated disorder is a neuropsychiatric disorder.
29. The method of Claim 28, wherein the neuropsychiatric disorder is bipolar affective disorder or schizophrenia.
30. The method of Claim 25, wherein the HKNG1 gene product comprises:
- (a) the amino acid sequence of SEQ ID NO:2;
  - (b) the amino acid sequence of SEQ ID NO:4;
  - (c) the amino acid sequence of SEQ ID NO:39;
  - (d) the amino acid sequence of SEQ ID NO:41;
  - (e) the amino acid sequence of SEQ ID NO:43;
  - (f) the amino acid sequence of SEQ ID NO:45;
  - (g) the amino acid sequence of SEQ ID NO:49;
  - (h) the amino acid sequence of SEQ ID NO:51;
  - (i) the amino acid sequence of SEQ ID NO:64; or
  - (j) the amino acid sequence of SEQ ID NO:66.
31. The method of Claim 25, wherein the individual is a mammal.
32. The method of Claim 31, wherein the mammal is a human.
33. A method for identifying a compound which modulates expression of an HKNG1 gene comprising:
- (a) contacting a test compound to a cell that expresses an HKNG1 gene;
  - (b) measuring a level of HKNG1 gene expression in the cell;
  - (c) comparing the level of HKNG1 gene expression in the cell in the presence of the test compound to a level of HKNG1 gene expression in the cell in the absence of the test compound,

wherein if the level of HKNG1 gene expression in the cell in the presence of the test compound differs from the level of expression of the HKNG1 gene in the cell in the absence of the test compound, a compound that modulates expression of an HKNG1 gene is identified.

34. The method of Claim 33, wherein the HKNG1 gene encodes an HKNG1 gene product comprising:

- (a) the amino acid sequence of SEQ ID NO:2;
- (b) the amino acid sequence of SEQ ID NO:4;
- (c) the amino acid sequence of SEQ ID NO:39;
- (d) the amino acid sequence of SEQ ID NO:41;
- (e) the amino acid sequence of SEQ ID NO:43;
- (f) the amino acid sequence of SEQ ID NO:45;
- (g) the amino acid sequence of SEQ ID NO:49;
- (h) the amino acid sequence of SEQ ID NO:51;
- (i) the amino acid sequence of SEQ ID NO:64; or
- (j) the amino acid sequence of SEQ ID NO:66.

35. The method of Claim 34, wherein the HKNG1 gene comprises:

- (a) the nucleotide sequence of SEQ ID NO:1;
- (a) the nucleotide sequence of SEQ ID NO:3;
- (a) the nucleotide sequence of SEQ ID NO:5;
- (a) the nucleotide sequence of SEQ ID NO:6;
- (a) the nucleotide sequence of SEQ ID NO:34;
- (a) the nucleotide sequence of SEQ ID NO:35;
- (a) the nucleotide sequence of SEQ ID NO:38;
- (a) the nucleotide sequence of SEQ ID NO:40;
- (a) the nucleotide sequence of SEQ ID NO:42;
- (a) the nucleotide sequence of SEQ ID NO:44;
- (a) the nucleotide sequence of SEQ ID NO:46;
- (a) the nucleotide sequence of SEQ ID NO:47;
- (a) the nucleotide sequence of SEQ ID NO:48; or
- (a) the nucleotide sequence of SEQ ID NO:65.

36. A method for identifying a compound which modulates expression or activity of an HKNG1 gene product comprising:

- (a) contacting a test compound to a cell that expresses an HKNG1 gene product;
- (b) measuring a level of HKNG1 gene product expression or activity in the cell;
- (c) comparing the level of HKNG1 gene product expression or activity in the cell in the presence of the test compound to a level of HKNG1 gene product expression or activity in the cell in the absence of the test compound,

wherein if the level of HKNG1 gene product expression or activity in the cell in the presence of the test compound differs from the level of HKNG1 gene product expression or activity in the cell in the absence of the test compound, a compound that modulates expression or activity of an HKNG1 gene product is identified.

37. The method of Claim 36, wherein the HKNG1 gene product comprises:

- (a) the amino acid sequence of SEQ ID NO:2;
- (b) the amino acid sequence of SEQ ID NO:4;
- (c) the amino acid sequence of SEQ ID NO:39;
- (d) the amino acid sequence of SEQ ID NO:41;
- (e) the amino acid sequence of SEQ ID NO:43;
- (f) the amino acid sequence of SEQ ID NO:45;
- (g) the amino acid sequence of SEQ ID NO:49;
- (h) the amino acid sequence of SEQ ID NO:51; or
- (i) the amino acid sequence of SEQ ID NO:64.

38. A method for identifying an individual having or at risk of developing a HKNG1-mediated disorder comprising the step of detecting the presence or absence of a polymorphism that correlates with an HKNG1 allele associated with the disorder, wherein presence of the polymorphism indicates that the individual has or is at risk of developing the HKNG1-mediated disorder.

39. The method of Claim 38, wherein the mutation results in production of a protein comprising an amino acid sequence that is different from the amino acid sequence of SEQ ID NO:2 or 4.

40. The method of Claim 39, wherein the mutation results in the substitution of a lysine for a glutamic acid at amino acid residue 202 of SEQ ID NO:2.

41. The method of Claim 39, wherein the mutation results in the substitution of a lysine for a glutamic acid at amino acid residue 184 of SEQ ID NO:4.

42. The method of Claim 36, wherein the method comprises the step of analyzing the sequence of the coding region of the human HKNG1 gene by preparing and sequencing cDNA comprising a sequence that hybridizes under stringent conditions to the complement of a nucleotide sequence which encodes the polypeptide sequence depicted in SEQ ID NO:2.